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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/622,088

07/18/2003

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IVGN 332

1853

65482 7590 12/28/2009
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EXAMINER

HORNING, MICHELLE S

ART UNIT

PAPER NUMBER

1648

MAIL DATE

DELIVERY MODE

12/28/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/622,088	Applicant(s) BENNETT ET AL.	
	Examiner MICHELLE HORNING	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 October 2009 and 03 November 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 45-56 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 45-56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/3/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This action is responsive to communication filed 10/26/2009 and 11/3/2009. The status of the claims is as follows: claims 45-56 are under current examination.

Any rejection or objection not reiterated herein has been withdrawn.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/26/2009 has been entered.

Information Disclosure Statement

The Information Disclosure Statement submitted 11/3/2009 has been considered and an initialed copy is attached to this action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 45-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 45 (*in part*) reads a packaging signal of the first nucleic acid molecule that is "present *in trans*" (see lines 15 and 16). The first nucleic acid molecule comprises the packaging signal (see part (a))

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and thus, the signal acts from the same molecule (*in cis*). It is not clear what is meant by “present *in trans*” in that what *in trans* is relative to is unclear. The instant specification describes packaging proteins encoded by the three additional nucleic acid molecules which encode retroviral proteins that are supplied *in trans*; see [00671]. However, this is not clear from the instant claims. The dependent claims fall herein.

In view of this provision, the claims (*in part*) are interpreted as the packaging signal of the first nucleic acid molecule is presented *in trans*.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 45-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Enablement is considered in view of the *Wands* factors.

Enablement is considered in view of the *Wands* factors.

Nature of the invention. The claims are drawn to a method of constructing a replication-incompetent recombinant retrovirus comprising: a) providing a first nucleic acid molecule lacking retroviral sequences which produce retroviral gene products and which comprises a 5'-LTR, a 3'-LTR, a packaging signal, and at least a first and a second recombination site that do not recombine with each;

b) contacting the first nucleic acid molecule with a second nucleic acid molecule comprising a sequence of interest flanked by at least a third and a fourth recombination site under conditions such that recombination occurs between the first and third recombination site and between the second and the fourth recombination site; and

c) introducing the nucleic acid molecule generated in step b), with at least three additional nucleic acid molecules which encode retroviral proteins, into a cell that packages the nucleic acid molecule generated in step b) such that the packaging signal of the first nucleic acid molecule is present *in trans*.

Scope of the invention. Claims 45-56 are broad in that they encompass constructing any retrovirus, any gene of interest and/or any recombination sites.

State of the prior art. von Melchner and Hoffken (*Blut*, 1988-previously cited) provide that the deletion of a packaging signal or psi residing in the LTRs leads to failure of virus assembly. Further, the presence of such a packaging signal is "absolutely required *in cis* position for particle production" (see p. 2, col. 2).

Working examples. Example 9 provides that retroviral packaging proteins including gag, pol and env are supplied in trans to allow the creation of replication incompetent viral particles capable of stably delivering a gene of interest; see[0671]. However, there are no examples which describe a packaging signal provided *in trans*.

Guidance in the specification. The specification provides the following recitation: "Deletion of the packing signal prevents packaging of the recombinant viral genome into retroviral particles, thus preventing spread of retroviral vectors to non-target cells in the event of infection with replication competent viruses"; see [0017].

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Predictability of the art. There is no way one could predict how to construct a replication-incompetent recombinant retrovirus by supplying the packaging signal *in trans* as claimed, given both the instant specification and the prior art teach that such a signal must be provided *in cis*.

Amount of experimentation necessary. Much undue experimentation would be necessary in order to construct a replication-incompetent recombinant retrovirus by supplying the packaging signal *in trans*, if even possible at all in view of both the instant specification itself and the prior art.

Given the discussion above, it would require undue experimentation for the ordinary artisan to perform the method as claimed.

Claims 45-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As discussed above, the specification fails to disclose a method of constructing a replication-incompetent recombinant retrovirus wherein a packaging signal is supplied *in trans*. [0017] of the instant specification provides that deletion of the packaging signal prevents successful packaging of the recombinant viral genome into retroviral particles. Separately, [0039] discloses that other packaging activities may be provided *in trans* including expressed from one or more plasmids. However, the instant specification provides no teaching to support a packaging signal *in trans* in the construction of a replication-incompetent

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recombinant retrovirus. In view of the lack of support in the instant specification, it appears that Applicant was not contemplating and therefore, not in possession of the invention as claimed.

Response to Arguments

Applicant's arguments with respect to claims 45-56 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELLE HORNING whose telephone number is (571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/M. H./
Examiner, Art Unit 1648

/Zachariah Lucas/
Primary Examiner, Art Unit 1648